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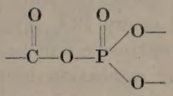
A quantum mechanical calculation of the electron distribution in carboxyl-phosphate and some related molecules

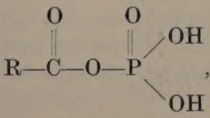
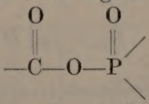
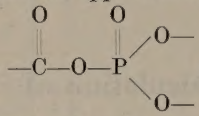
By Barbro Grabe

With 3 figures in the text

SUMMARY

The electron distribution in the  $-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{P}}\begin{smallmatrix}\diagup O-\\ \diagdown O-\end{smallmatrix}$ group of the carboxyl-phosphate molecule has been calculated by a semi-empirical method. Six electrons are taken into consideration explicitly, viz. two π-electrons of the $C=O$ double bond, the lone pair at the bridge O-atom and two electrons of the phosphoryl group, corresponding to the usual π-approximation. For comparison, the electron distribution in the carboxyl ion, in the phosphate ion and in polyphosphates of the same type as adenosine diphosphate and triphosphate have been calculated. It appears from the calculations that the charges due to the "π-electrons" on the C- and P-atoms respectively are approximately the same for all the molecules considered. The charges on the bridge O-atoms in carboxyl-phosphate and in the polyphosphates are on the other hand very different from the charges on the other O-atoms of the same group and also from the charges on the O-atoms of the carboxyl and phosphate ions. The possibility of explaining some experimental data, by means of the results obtained, concerning energy transfer in the living cell is discussed.

1. Introduction

Carboxyl-phosphate,  $R-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{P}}\begin{smallmatrix}\diagup OH\\ \diagdown OH\end{smallmatrix}$, can be considered as a representative of a group of compounds in the living cell which make possible a certain type of energy transfer. These compounds are called high-energetic since relatively much energy is released when they are hydrolyzed. Kalckar [1] and Oesper [2] have pointed out the significance of "opposing resonance" for their high energy content; e.g. in carboxyl-phosphate, opposing resonance in the  $-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{P}}\begin{smallmatrix}\diagup \\ \diagdown \end{smallmatrix}$ group is significant. However, as far as the author is aware, no quantum chemical calculation of the electron distribution has been performed previously. As such a calculation could be of interest and of importance for the understanding of the energy transfer in the living cell, the author has made an approximate calculation of the electron density at the different atoms of the  group. For comparison, the electron distribution is calculated for the carboxyl ion and phosphate ion as well as for polyphosphates of the types, adenosine diphosphate (ADP) and adenosine triphosphate (ATP). These calculations are reported in the present paper. Some implications concerning the energy transfer have been discussed in two other papers [3, 4], in which preliminary results of the present calculations were used.

2. Method

The semi-empirical method used here is the same as that used by Fischer [5]. Only six of the electrons involved could be taken into consideration explicitly, viz. two π-electrons of the C=O double bond, the lone pair at the bridge oxygen atom and two electrons of the phosphoryl group PO_3. This approximation corresponds to the usual π-approximation. Consequently we will call the dislocalized orbitals of the carboxyl-phosphate "π-orbitals", the quotation marks indicating that the orbitals are not π-orbitals in the usual sense.

The calculation has been carried out by the molecular orbital method. Atomic orbitals (AO's) have been adopted for all the atoms of the group and molecular orbitals (MO's) have been approximated by linear combination of atomic orbitals (LCAO-MO). An MO Ψ_j over a group of the atoms λ, μ ... can be expressed as

$$\Psi_j = \sum_{\lambda} c_{j\lambda} \varphi_{\lambda}, \tag{1}$$

where φ_λ is a normalized AO of the λth atom and the $c_{j\lambda}$ are parameters. Normalization of the MO's gives

$$\int \Psi_j^* \Psi_j \, d\tau = \sum_{\lambda,\mu} c_{j\lambda} c_{j\mu} S_{\lambda\mu} = 1, \tag{2}$$

where

$$S_{\lambda\mu} = \int \varphi_\lambda^* \varphi_\mu \, d\tau. \tag{3}$$

Then the energy of an electron in the jth MO is

$$\varepsilon_j = \int \Psi_j^* H \Psi_j \, d\tau, \tag{4}$$

where H is a one-electron Hamiltonian. The parameters $c_{j\lambda}$ are as usual determined by minimizing the energy (4), which gives the condition

$$|H_{\lambda\mu} - \varepsilon S_{\lambda\mu}| = 0 \tag{5}$$

where

$$H_{\lambda\mu} = \int \varphi_\lambda^* H \varphi_\mu \, d\tau. \tag{6}$$

Each root ε of equation (5) corresponds to a molecular orbital, i.e. to a set of c-parameters.

Table 1. Ionization energies in eV, taken from Skinner and Pritchard [6].

I_λ is the ionization energy required to remove a p electron from atom λ, the atom being in the ground state.

I_C	11.26	$I_C - I_O$	-2.35
I_O	13.61	$I_P - I_O$	-2.63
I_P	10.98	$I_C - I_P$	$+0.28$

We now introduce the following notations

$$H_{\lambda\lambda} = \alpha_\lambda, \qquad H_{\lambda\mu} = \beta_{\lambda\mu}, \tag{7}$$

$$\gamma_{\lambda\mu} = \beta_{\lambda\mu} - \tfrac{1}{2} S_{\lambda\mu} (\alpha_\lambda + \alpha_\mu), \tag{8}$$

$$\alpha_\lambda - \alpha_\mu = 2\,\delta_{\lambda\mu}, \tag{9}$$

$$\alpha_C - \varepsilon = z. \tag{10}$$

The index C in (10) indicates that the quantity is referred to a carbon atom. Introducing (7)–(10) into equation (5) we obtain

$$\begin{vmatrix} z + 2\,\delta_{1C} & \gamma_{12} + S_{12}(z + \delta_{1C} + \delta_{2C}) & 0 & \cdots & \cdots \\ \gamma_{12} + S_{12}(z + \delta_{1C} + \delta_{2C}) & z + 2\,\delta_{2C} & \gamma_{23} + S_{23}(z + \delta_{2C} + \delta_{3C}) & 0 & \cdots \\ 0 & \gamma_{23} + S_{23}(z + \delta_{2C} + \delta_{3C}) & z + 2\,\delta_{3C} & \cdots & \cdots \\ \cdot & \cdot & \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot & \cdot & \cdot \end{vmatrix} = 0 \tag{11}$$

According to the semi-empirical method used here, the values of the integrals $\delta_{\lambda\mu}$ and $\gamma_{\lambda\mu}$ should be determined from their connection with experimental data. Inserting these values in (11), this equation in z can be solved. The MO's can then be obtained from a calculation of the sets of c-parameters, one set corresponding to each z-value.

The experimentally determined quantity that most closely corresponds to the integral $\delta_{\lambda\mu}$ may be half the difference between the ionization energies of the atoms μ and λ, but there is no exact correspondence. Upon deliberation, however, it seemed that $|2\delta_{\lambda\mu}|$ should be somewhat smaller than $|I_\mu - I_\lambda|$. Therefore it appeared necessary to make several calculations, differing only in the $\delta_{\lambda\mu}$ values used, to obtain an

Table 2. $2\,\delta_{\lambda\mu}$ values (in eV) used in the calculations.

Calculations denoted	A	B	C	D
$2\,\delta_{OC}$	-1.0	-1.4	-1.6	-2.0
$2\,\delta_{OP}$	-1.4	-1.8	-1.8	-2.2
$2\,\delta_{PC}$	$+0.4$	$+0.4$	$+0.2$	$+0.2$

insight into the dependence of the results on the $\delta_{\lambda\mu}$ values. Ionization energies given by Skinner and Pritchard [6] are listed in Table 1 and the $\delta_{\lambda\mu}$ values used in the calculations are listed in Table 2.

The quantities $\gamma_{\lambda\mu}$ have been obtained from experimentally determined bond energies in the following manner.

Let us consider a localized MO extending only over the two atoms λ and μ. The distance between the atoms λ and μ is assumed to be the same as in the group with dislocalized orbitals since it is for this distance that we wish to calculate $\gamma_{\lambda\mu}$. Hence, we are considering a hypothetical case. When equation (11) is solved for this case, we obtain

$$z = -\delta_{\lambda C} - \delta_{\mu C} + \frac{1}{1 - S_{\lambda\mu}^2}\left[\gamma_{\lambda\mu} S_{\lambda\mu} \pm \sqrt{\gamma_{\lambda\mu}^2 + \delta_{\lambda\mu}^2 (1 - S_{\lambda\mu}^2)}\right]. \tag{12}$$

Here only the root with the positive sign is of interest since this root corresponds to the MO of lowest energy.

To obtain a quantity that can be calculated from experimental data, it is convenient to form the expression $D' = \alpha_\lambda + \alpha_\mu - 2\varepsilon$. Then from (9), (10) and (12) we obtain

$$D' = \frac{2}{1 - S_{\lambda\mu}^2}\left[\gamma_{\lambda\mu} S_{\lambda\mu} + \sqrt{\gamma_{\lambda\mu}^2 + \delta_{\lambda\mu}^2 (1 - S_{\lambda\mu}^2)}\right]. \tag{13}$$

This gives

$$\gamma_{\lambda\mu} = -\frac{D' S_{\lambda\mu}}{2} \pm \sqrt{\frac{D'^2}{4} - \delta_{\lambda\mu}^2} \tag{14}$$

for the determination of $\gamma_{\lambda\mu}$. Of the two values, the negative one corresponds to the definition of $\gamma_{\lambda\mu}$ in (8).

To determine $\gamma_{\lambda\mu}$ from (14), the values of D', $S_{\lambda\mu}$ and $\delta_{\lambda\mu}$ must be known. In a treatment of π-electrons, D' is approximately equal to the difference between the dissociation energies of a double bond and a single bond, the interatomic distance in both cases being the same, viz. the distance to which the $\gamma_{\lambda\mu}$ and $S_{\lambda\mu}$ are referred. In the calculation of $\gamma_{\lambda\mu}$ for a σ-bond, D' is approximately equal to the dissociation energy of a σ-bond with the interatomic distance to which $\gamma_{\lambda\mu}$ and $S_{\lambda\mu}$ are referred. To calculate the dissociation energy D_r for an arbitrary distance r between the atoms when the dissociation energy D_0 for the equilibrium distance r_0 is known, the Morse curve

$$D_0 - D_r = D_0 [1 - e^{-a(r - r_0)}]^2 \qquad [15]$$

has been used. Here $a = \sqrt{k/2D_0}$, k being the force constant. Unfortunately all the necessary experimental values for the force constants k and dissociation energies D_0 could not be found in the literature. Cottrell's tables [7] and the values reported in Fischer [5] have been used for the estimation of the values used in the present calculation. These latter values are listed in Table 3 and the D_r values calculated from (15) are given in Table 4.

To obtain values for the overlap integrals $S_{\lambda\mu}$, the explicit form of the AO's, φ_λ, must be fixed. The AO's used in the calculations are given in section 3. When possible, the values of the overlap integrals have been obtained by interpolation in Mulliken's tables [8]. The remaining values have been calculated by means of Rosen's A and

Table 3. Values used for the calculation of D_r.

	O–C		O–P	
	Single bond	Double bond	Single bond	Double bond
r_0 in Å	1.43	1.21	1.66	1.39
Dissociation energy D_0, Kcal/mole	80	156	80	156
Force constant k, dyne/cm	$4.4 \cdot 10^5$	$12.0 \cdot 10^5$	$4 \cdot 10^5$	$11 \cdot 10^5$

B functions, which have recently been tabulated by Flodmark [9] for an extensive range of parameter values. All of the $S_{\lambda\mu}$ values obtained are given in Table 5.

D_r values from Table 4, $S_{\lambda\mu}$ values from Table 5 and $\delta_{\lambda\mu}$values from Table 2 have been inserted into equation (14) for the calculation of $\gamma_{\lambda\mu}$. The negative values of $\gamma_{\lambda\mu}$ thus obtained are given in Table 5.

The $\gamma_{\lambda\mu}$ values calculated in this way have been inserted into equation (11) together with values for $\delta_{\lambda\mu}$ and $S_{\lambda\mu}$. This equation was then solved by means of the Swedish electronic computer Besk, thus giving z-values and the parameters $c_{j\lambda}$.

The energy values (4) were obtained from the z-values according to (10). The value for α_C was assumed to be -11.26 eV according to [6], see Table 1.

The charges on the atoms, arising from the electrons considered in the present calculation of MO's, have been computed by means of Mulliken's definition [10]. For this reason, two populations, which are defined by Mulliken in the following manner, have been calculated. The partial gross population $N(j;\lambda)$ in a singly occupied MO, Ψ_j, and AO, φ_λ, is defined by

$$N(j;\lambda) = c_{j\lambda}^2 + \sum_{\mu} c_{j\lambda} c_{j\mu} S_{\lambda\mu}. \tag{16}$$

The summation over μ has been carried out over only the nearest neighbours of the atom λ. The gross atomic population $N(\lambda)$ on the atom λ, expressed here for doubly occupied space orbitals since there are 2 electrons in each orbital considered, is defined by

$$N(\lambda) = 2\sum_{j} N(j;\lambda) = 2\sum_{j} c_{j\lambda}^2 + 2\sum_{j}\sum_{\mu} c_{j\lambda} c_{j\mu} S_{\lambda\mu}, \tag{17}$$

Table 4. Dissociation energies calculated from values in Table 3 according to (15).

Distances between C and O, in Å	C=O Kcal/mole	C–O Kcal/mole	Distances between P and O, in Å	P=O Kcal/mole	P–O Kcal/mole
1.21	—	56	1.45	154	61
1.23	156	61	1.50	148	70
1.28	152	70	1.55	142	76
1.40	136	80	1.60	134	79
1.43	131	—			

Table 5. Calculated values for $S_{\lambda\mu}$ and $\gamma_{\lambda\mu}$ where $\gamma_{\lambda\mu}$ is calculated according to (14) and given in eV.

Values used for the orbital constant ζ_P and for $\delta_{\lambda\mu}$ (in eV) are given. For further information about AO's used, see section 3.

Distance between C and O, in Å	1.21	1.23	1.28	1.40	1.43
$S_{OC}(2p\pi, 2p\pi)$	0.294	0.284	0.260	0.213	0.200
$\gamma_{OC}(2p\pi, 2p\pi)$ for					
$2\delta_{OC} = -1.0$	-2.75	-2.58	-2.17	-1.37	-1.19
$2\delta_{OC} = -1.4$	-2.69	—	-2.10	—	-1.06
$2\delta_{OC} = -1.6$	-2.65	—	-2.05	—	-0.97
$2\delta_{OC} = -2.0$	-2.56	—	-1.94	—	-0.67

Distance between P and O, in Å	1.45	1.50	1.55	1.60
$S_{OP}(2p\sigma, 3p\sigma)$ for				
$\zeta_P = 1.72$	—	0.319	0.321	—
$\zeta_P = 1.60$	0.290	—	0.305	—
$S_{OP}(2p\pi, 3p\pi)$ for				
$\zeta_P = 1.72$	—	—	—	0.188
$\zeta_P = 1.60$	—	—	0.218	0.200
$S_{OP}(2p\pi, 4p\pi)$ for				
$\zeta_P = 0.43$	—	0.037	0.038	0.038
$\gamma_{OP}(2p\sigma, 3p\sigma)$ for $2\delta_{OP} = -1.4$ and				
$\zeta_P = 1.72$	—	-1.83	-2.01	—
$\zeta_P = 1.60$	-1.51	—	-1.99	—
$\gamma_{OP}(2p\pi, 3p\pi)$ for $2\delta_{OP} = -1.4$ and				
$\zeta_P = 1.72$	—	—	—	-1.19
$\zeta_P = 1.60$	—	—	-1.56	-1.20
$\gamma_{OP}(2p\pi, 4p\pi)$ for $\zeta_P = 0.43$ and				
$2\delta_{OP} = -1.4$	—	-1.63	-1.30	-1.01
$2\delta_{OP} = -1.8$	—	-1.52	-1.17	-0.83
$2\delta_{OP} = -2.2$	—	-1.38	-0.97	-0.51

where the summation over j should be carried out over the occupied space orbitals and where the summation over μ is as in (16). The charge $Q(\lambda)$ on the atom λ is defined as

$$Q(\lambda) = N_0(\lambda) - N(\lambda), \tag{18}$$

where $N_0(\lambda)$ is the number of electrons in the analogous orbitals of the neutral atom.

3. Choice of AO's and the geometry of the molecules

In the present application of the method described above to the "π-electrons" of the carboxyl-phosphate, several calculations have been made which differ in the orbitals adopted for the phosphoryl group and in the estimate of interatomic distances. The different assumptions are collected in Tables 6 and 7 and will now be briefly discussed.

For the O-atoms and the C-atom $2p$, hydrogen-like orbitals have been adopted

$$\varphi_{2p} = 2\sqrt{\frac{\zeta^5}{3}}\, r\, e^{-\zeta r}\, Y(\vartheta, \varphi). \tag{19}$$

The ζ-values used are 1.88 for oxygen [11] and 1.56 for carbon [5].

For the P-atom, the following kinds of orbitals have been used:

(a) in calculations I, II, IV and V, a $3p$ analytical orbital

$$\varphi_{3p} = \frac{2}{3}\sqrt{\frac{2\,\zeta^7}{5}}\, r^2 e^{-\zeta r}\, Y(\vartheta, \varphi), \tag{20}$$

where $\zeta = 1.60$ in calculations I and II and $\zeta = 1.72$ in IV and V, and

(b) in calculations III and VI, a $4p$ analytical orbital

$$\varphi_{4p} = \frac{2}{3}\sqrt{\frac{\zeta^9}{35}}\, r^3 e^{-\zeta r}\, Y(\vartheta, \varphi), \tag{21}$$

where $\zeta = 0.43$.

The ζ-values for the P-atom have been calculated according to Slater. The value 1.60 refers to the shielding of a $3p$ electron when the configuration is $1s^2 2s^2 2p^6 3s^2 3p^3$, the value 1.72 to a $3p$ electron when the configuration is $1s^2 2s^2 2p^6 3s^1 3p^3 3d^1$ and the value 0.43 to a $4p$ electron when the configuration is $1s^2 2s^2 2p^6 3s^1 3p^3 4p^1$.

The spatial location of the different atoms is given in Fig. 1. The O_α-atom, the C-atom, the O_β-atom, i.e. the bridge atom, and the P-atom are assumed to be in the xy-plane. The atomic orbitals used for these atoms are p_z orbitals. The O_β and the three O_γ atoms are situated at the corners of a tetrahedron around P.

In the calculations II, IV and V, it has been assumed that the three O-atoms denoted γ form a group called $(O_3)_\gamma$. For this group, the orbital

$$\varphi_{0\gamma} = \sqrt{\frac{2}{3}}\left[\varphi(2p\sigma_{\gamma 1}) - \frac{1}{2}\{\varphi(2p\sigma_{\gamma 2}) + \varphi(2p\sigma_{\gamma 3})\}\right] \tag{22}$$

has been used. $2p\sigma_{\gamma n}$ represents a $2p$ orbital of $O_{\gamma n}$ in the direction of the σ-bond of $P\text{–}O_{\gamma n}$. The orbital (22) is of the same symmetry as the orbitals of the atoms C, O_α and O_β when $P\text{–}O_{\gamma 1}$ is in the yz-plane (see Fig. 1a). In the other calculations, only one of the O_γ-atoms, $O_{\gamma 1}$, has been included in the calculation. In calculation I, $O_{\gamma 1}$ is assumed to be situated in the yz-plane and, in calculations III and VI, in the xy-plane (see Fig. 1b). The $2p_z$ orbital has been used for $O_{\gamma 1}$.

The calculations for the carboxyl ion, the phosphate ion and the polyphosphates of the types, adenosine diphosphate (ADP) and adenosine triphosphate (ATP), have been made using the same parameter values as in certain of the above-mentioned

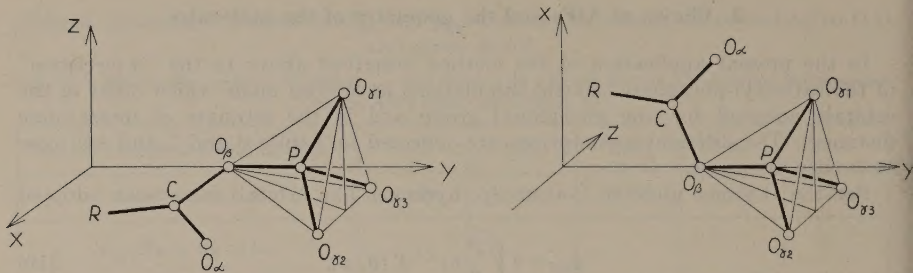
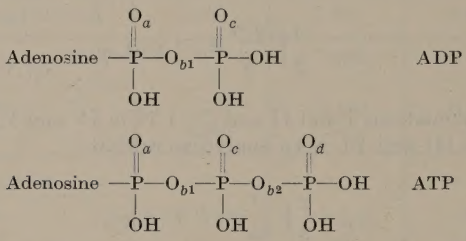


Fig. 1*a* Fig. 1*b*

Fig. 1. O_α, C, O_β and P are in the *xy*-plane. (*a*) P–O_{γ_1} is in the *yz*-plane. Calculations I, II, IV and V. (*b*) P–O_{γ_1} is in the *xy*-plane. Calculations III and VI.



$$\text{Adenosine}-\underset{\underset{\text{OH}}{|}}{\overset{\overset{\text{O}_a}{\|}}{\text{P}}}-\text{O}_{b1}-\underset{\underset{\text{OH}}{|}}{\overset{\overset{\text{O}_c}{\|}}{\text{P}}}-\text{OH} \qquad \text{ADP}$$

$$\text{Adenosine}-\underset{\underset{\text{OH}}{|}}{\overset{\overset{\text{O}_a}{\|}}{\text{P}}}-\text{O}_{b1}-\underset{\underset{\text{OH}}{|}}{\overset{\overset{\text{O}_c}{\|}}{\text{P}}}-\text{O}_{b2}-\underset{\underset{\text{OH}}{|}}{\overset{\overset{\text{O}_d}{\|}}{\text{P}}}-\text{OH} \qquad \text{ATP}$$

Fig. 2. The notations of the atoms in adenosine diphosphate and adenosine triphosphate.

calculations for carboxyl-phosphate. The parameter values for all the different molecules are summarized in Table 6.

The interatomic distances in the calculations have been estimated from known distances for pure single and double bonds and from distances in the carboxyl ion and the phosphate ion. The distances used in the calculations are listed in Table 7.

4. Results

In Table 8, the gross atomic population $N(\lambda)$ according to (17) and the charge $Q(\lambda)$ according to (18) due to the "π-electrons" for each atom are given. The summation over j in (17) must be taken over a different number of MO's for the different molecules: (i) for carboxyl-phosphate and adenosine diphosphate, over the three lowest orbitals, (ii) for the carboxyl ion and the phosphate ion, over the two lowest orbitals, and (iii) for adenosine triphosphate, over the five lowest orbitals. In the calculation of $Q(\lambda)$, the $N_0(\lambda)$-value used is equal to 1 in all cases except for the bridge O-atoms, i.e. O_β in the carboxyl-phosphate, O_{b_1} in ADP and O_{b_1} and O_{b_2} in ATP. For these bridge O-atoms, $N_0(\lambda)$ is equal to 2 since a lone pair, which belongs to the neutral atom, is considered.

Table 9 shows the calculated energy values in eV. The ε-values were obtained from equation (10), the value for α_C being assumed to be -11.26 eV.

Table 10 in the Appendix contains the partial gross population $N(j;\lambda)$ defined in (16).

Table 6. General summary of atomic orbitals adopted in the calculations.

Calculations I–VI refer to carboxyl-phosphate. O_α, C, O_β and P are situated approximately in the xy-plane. For the notations concerning the atoms, see Figs. 1 and 2. Orbital exponent denoted by ζ.

		O_α	C	O_β	P	$O_{\gamma 1}$	$(O_3)_\gamma$
Calc. I	Orbital ζ	$2p_z$ 1.88	$2p_z$ 1.56	$2p_z$ 1.88	$3p_z$ 1.60	$2p_z$, σ-bond 1.88	—
Calc. II	Orbital ζ	As in calc. I „			$3p_z$ 1.60	—	φ_{gr} of (22) 1.88
Calc. III, VI	Orbital ζ	„ „			$4p_z$ 0.43	$2p_z$, π-bond 1.88	—
Calc. IV, V	Orbital ζ	„ „			$3p_z$ 1.72	—	φ_{gr} of (22) 1.88
Calc. VII Carboxyl ion	Orbital ζ	„ „					
Calc. VIII Phosphate ion	Orbital ζ			$2p_z$ 1.88	$3p_z$ 1.60	—	φ_{gr} of (22) 1.88
Calc. IX Phosphate ion	Orbital ζ			$2p_z$ 1.88	$4p_z$ 0.43	$2p_z$, π-bond 1.88	—
Calc. X, XI ADP and ATP	Orbital ζ			$2p_z$ ([a]) 1.88	$4p_z$ ([b]) 0.43		

[a] For all the O-atoms. π-Bonds between the P and O atoms. [b] For all the P-atoms.

Table 7. Distances adopted in the calculations (in Å).

The notations for the atoms are given in Figs. 1 and 2.

	Calculation	Distances in Å				ζ_P
		O_α–C	C–O_β	O_β–P	P–O_γ	
Carboxyl-phosphate	I	1.21	1.43	1.60	1.45	1.60
	II	1.21	1.43	1.60	1.55	1.60
	III	1.21	1.43	1.55	1.55	0.43
	IV	1.21	1.43	1.60	1.55	1.72
	V	1.23	1.40	1.60	1.50	1.72
	VI	1.23	1.40	1.60	1.50	0.43
Carboxyl ion	VII	1.28	1.28			
Phosphate ion	VIII			1.55	1.55	1.60
	IX			1.55	1.55	0.43
ADP, ATP	X, XI			1.60[a]	1.50[b]	0.43

[a] Distances P–O_{b1} and P–O_{b2}. [b] Distances P–O_a, P–O_c and P–O_d.

Table 8. $N(\lambda)$ and $Q(\lambda)$ due to the "π-electrons", calculated according to (17) and (18).

For the notations for the atoms, see Figs. 1 and 2. The calculations I–VI refer to carboxyl-phosphate, VII to the carboxyl ion, VIII and IX to the phosphate ion and X and XI to polyphosphates of the types ADP and ATP. For further information about the import of the numeration of the calculations, see the last two columns and also Tables 6 and 7.

Carboxyl-phosphate, carboxyl ion and phosphate ion

Calc.	$N(O_\alpha)$	$Q(O_\alpha)$	$N(C)$	$Q(C)$	$N(O_\beta)$	$Q(O_\beta)$	$N(P)$	$Q(P)$	$N(O_{\gamma1})$	$Q(O_{\gamma1})$	$N(O_3)_\gamma$	$Q(O_3)_\gamma$	ζ_P	Orb. of $(O_3)_\gamma$
A. $2\delta_{OC} = -1.0$ eV; $2\delta_{OP} = -1.4$ eV														
I	1.28	−0.28	0.83	+0.17	1.67	+0.33	0.65	+0.35	1.58	−0.58	—	—	1.60	—
II	1.29	−0.29	0.83	+0.17	1.73	+0.27	0.74	+0.26	—	—	1.41	−0.41	1.60	φ_{gr} of (22)
III	1.27	−0.27	0.83	+0.17	1.61	+0.39	0.64	+0.36	1.66	−0.66	—	—	0.43	—
IV	1.29	−0.29	0.83	+0.17	1.74	+0.26	0.74	+0.26	—	—	1.40	−0.40	1.72	φ_{gr} of (22)
V	1.34	−0.34	0.83	+0.17	1.69	+0.31	0.72	+0.28	—	—	1.43	−0.43	1.72	φ_{gr} of (22)
VI	1.34	−0.34	0.82	+0.18	1.68	+0.32	0.65	+0.35	1.50	−0.50	—	—	0.43	—
VII	1.58	−0.58	0.84	+0.16	1.58	−0.58								
VIII					1.77	−0.77	0.75	+0.25	—	—	1.48	−0.48	1.60	φ_{gr} of (22)
IX					1.68	−0.68	0.64	+0.36	1.68	−0.68	—	—	0.43	—
B. $2\delta_{OC} = -1.4$ eV; $2\delta_{OP} = -1.8$ eV														
III	1.33	−0.33	0.76	+0.24	1.68	+0.32	0.52	+0.48	1.73	−0.73			0.43	
VII	1.62	−0.62	0.77	+0.23	1.62	−0.62								
IX					1.74	−0.74	0.52	+0.48	1.74	−0.74			0.43	
C. $2\delta_{OC} = -1.6$ eV; $2\delta_{OP} = -1.8$ eV														
III	1.35	−0.35	0.72	+0.28	1.69	+0.31	0.52	+0.48	1.73	−0.73			0.43	
VII	1.63	−0.63	0.73	+0.27	1.63	−0.63								
IX = IXB					1.74	−0.74	0.52	+0.48	1.74	−0.74			0.43	
D. $2\delta_{OC} = -2.0$ eV; $2\delta_{OP} = -2.2$ eV														
III	1.40	−0.40	0.64	+0.36	1.78	+0.22	0.37	+0.63	1.81	−0.81			0.43	
VII	1.67	−0.67	0.65	+0.35	1.67	−0.67								

Calc.	$N(O_a)$	$Q(O_a)$	$N(P)$	$Q(P)$	$N(O_{b1})$	$Q(O_{b1})$	$N(P)$	$Q(P)$	$N(O_c)$	$Q(O_c)$	$N(O_{b2})$	$Q(O_{b2})$	$N(P)$	$Q(P)$	$N(O_d)$	$Q(O_d)$
A. $2\delta_{OP} = -1.4$ eV																
X	1.50	−0.50	0.65	+0.35	1.69	+0.31	0.65	+0.35	1.50	−0.50						
XI	1.51	0.51	0.65	+0.35	1.71	+0.29	0.68	+0.32	1.58	−0.58	1.71	+0.29	0.65	+0.35	1.51	−0.51
B = C. $2\delta_{OP} = -1.8$ eV																
X	1.58	0.58	0.53	+0.47	1.78	+0.22	0.53	+0.47	1.58	−0.58						
XI	1.58	0.58	0.53	+0.47	1.79	+0.21	0.57	+0.43	1.63	−0.63	1.79	+0.21	0.53	+0.47	1.58	−0.58
D. $2\delta_{OP} = -2.2$ eV																
X	1.65	−0.65	0.40	+0.60	1.91	+0.09	0.40	+0.60	1.65	−0.65						
XI	1.65	−0.65	0.40	+0.60	1.91	+0.09	0.42	+0.58	1.67	−0.67	1.91	+0.09	0.40	+0.60	1.65	−0.65

Table 9. ε-values (in eV) obtained from z-values according to (10).

The numeration of the calculations indicates the type of AO's used and the distances between the atoms (see Tables 6 and 7), while the notation A, B ... indicates the $\delta_{\lambda\mu}$ values used. The $\delta_{\lambda\mu}$ values are given in eV.

Calc.	Carboxyl-phosphate								
	I	II	III	IV	V	VI	III		
	A						B	C	D
$2\delta_{OC}$	−1.0						− 1.4	− 1.6	− 2.0
$2\delta_{OP}$	−1.4						− 1.8	− 1.8	− 2.2
Orb. 1	−14.0	−14.0	−14.1	−14.0	−14.0	−14.0	−14.2	−14.3	−14.4
2	−13.1	−13.5	−13.4	−13.5	−13.3	−13.4	−13.5	−13.7	−13.8
3	−12.3	−12.3	−12.3	−12.3	−12.3	−12.3	−12.7	−12.9	−13.3
4	− 8.8	− 7.9	− 9.6	− 7.8	− 8.1	− 9.5	− 9.9	−10.1	−10.4
5	− 6.7	− 6.3	− 7.0	− 6.3	− 6.4	− 7.1	− 7.4	− 7.5	− 8.0

Calc.	Carboxyl ion				Phosphate ion				
	VII				VIII	IX			
	A	B	C	D	A	A	B	C	D
$2\delta_{OC}$	− 1.0	− 1.4	− 1.6	− 2.0	− 1.0	− 1.0	− 1.4	− 1.6	− 2.0
$2\delta_{OP}$	—	—	—	—	− 1.4	− 1.4	− 1.8	− 1.8	− 2.2
Orb. 1	−14.0	−14.2	−14.3	−14.4	−13.6	−13.4	−13.6	−13.8	−13.9
2	−12.3	−12.7	−12.9	−13.3	−12.3	−12.3	−12.7	−12.9	−13.3
3	− 6.9	− 7.2	− 7.4	− 7.8	− 6.7	− 9.5	− 9.8	−10.0	−10.3

Calc.	Adenosine diphosphate				Adenosine triphosphate				
	X				XI				
	A	B	C	D	A	B	C	D	
$2\delta_{OC}$	− 1.0	− 1.4	− 1.6	− 2.0	− 1.0	− 1.4	− 1.6	− 2.0	
$2\delta_{OP}$	− 1.4	− 1.8	− 1.8	− 2.2	− 1.4	− 1.8	− 1.8	− 2.2	
Orb. 1	−13.7	−13.8	−14.0	−14.0	−13.9	−13.9	−14.1	−14.0	
2	−13.3	−13.5	−13.7	−13.9	−13.5	−13.6	−13.8	−13.9	
3	−12.3	−12.7	−12.9	−13.3	−13.3	−13.5	−13.7	−13.9	
4	− 9.7	− 9.9	−10.1	−10.3	−12.3	−12.7	−12.9	−13.3	
5	− 9.1	− 9.5	− 9.7	−10.2	−12.3	−12.7	−12.9	−13.3	
6	—	—	—	—	− 9.7	− 9.9	−10.1	−10.3	
7	—	—	—	—	− 9.4	− 9.7	− 9.9	−10.3	
8	—	—	—	—	− 8.9	− 9.3	− 9.5	−10.1	

5. Discussion

The semi-empirical method described above is unfortunately approximate in several respects. Firstly, all the necessary empirical data have not been determined experimentally so that some of them must be estimated with guidance from other existing data. Furthermore there is no quantity that can be determined experimentally which really corresponds to the δ-integrals. Another point is that it is difficult to choose appropriate orbitals for the P-atom and thus for the phosphoryl group. For this reason, it seemed to be necessary to examine the influence on the results of the different parameters in equation (11).

Two types of variation have been made: (*a*) Calculations have been performed in which the values assumed for the interatomic distances and the AO's chosen for the phosphoryl group were different. In all these calculations (calc. IA–VIA), the same values for the δ's were used, and thus only the non-diagonal elements in (11) were varied. (*b*) The same interatomic distances and AO's as in IIIA were used but the δ-values were varied (calc. IIIB, IIIC and IIID) and hence all the elements in (11) were therefore varied. This latter type of variation was also performed for the carboxyl ion, the phosphate ion and the polyphosphates.

It is seen that the variations of type (*a*) had only a relatively small influence on the results. The characteristics of the distribution of the charges between the atoms is the same in all the cases (see Table 8).

The variations in the δ-values had a greater influence on the charges on the atoms. It is seen from Table 8 that the positive charges on the bridge O-atoms in the carboxyl-phosphate and the polyphosphates decrease when more negative δ-values are chosen while the negative charges on the other O-atoms simultaneously increase. In all the calculations, however, the charges on the bridge O-atoms are very different from the charges on the other O-atoms considered, viz. the other O-atoms in the same group as well as those in the simple carboxyl and phosphate ions. These differences in charge remain approximately unchanged when the δ-values are varied. For all of the δ-values used in the present calculations, the bridge O-atoms are positively charged and the charges are considerable in all the cases except XD and XID.

It seems probable that the correct δ-values are within the range of values used in the calculations. When using the D_r-values of Table 4, larger δ-values cannot be used in the calculation of γ according to (14) since the quantity under the radical sign then becomes negative. In other cases, when other D_r-values are used, there is of course the possibility of using larger δ-values.

Furthermore, it appears from Table 8 that the charges obtained on C and P respectively in carboxyl-phosphate and the polyphosphates are approximately the same as the charges on the corresponding atoms in the simple carboxyl and phosphate ions when the same AO's and δ-values are used in the calculations. (Compare III, VII, IX, X and XI for each δ-value.)

The results of the calculations of the charges *due to the "π-electrons"* can be summarized as follows. The charges on the C-atom and the P-atoms in the carboxyl-phosphate and the polyphosphates are the same as on the corresponding atoms in the carboxyl and phosphate ions. The charges on the bridge O-atoms in the carboxyl-phosphate and the polyphosphates, however, are very different from the charges on the other O-atoms of the same group and from the charges on the O-atoms of the carboxyl and phosphate ions, all of the non-bridge charges being much more negative. Furthermore it seems very probable that the charges on the bridge O-atoms are positive and of considerable magnitude.

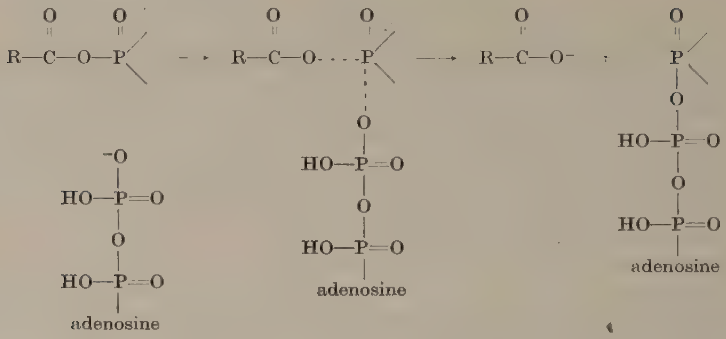


Fig. 3. An ADP ion attacking carboxyl-phosphate, resulting in the formation of a carboxyl ion and ATP.

These results seem to give information which is adequate for the purpose of this investigation, viz. to gain an insight into the mechanism of the transfer of energy in the living cell. It is well known that, when carboxyl-phosphate reacts with other molecules, either the P–O bond or the C–O bond can be broken. For example, when it reacts with adenosine diphosphate (ADP), the P–O bond is broken and adenosine triphosphate (ATP) and carboxyl ion are formed. This is a reaction which requires an activated phosphoryl group. In reactions requiring activated acetyl groups, however, the C–O bond is broken.

Using the results of the present calculations, these experimental data can be explained in the following manner. Since oxygen is a very electronegative atom, the existing distribution of the "π-electrons" undoubtedly causes the σ-electrons in the σ-bonds between the bridge O-atom and the C- and P-atoms to be attracted closer to the O-atom than in the simple carboxyl and phosphate ions.[1] But this is not possible without making the C- and P-atoms more positive than in the simple ions. Thus, the three atoms in the –C–O–P– group compete for the electrons. This stabilizes the molecule and causes the so-called high-energy of the molecule. When the C-atom or the P-atom is attacked by a negative ion, the σ-electrons of the bond between the attacked atom and the bridge O-atom are displaced towards the O-atom and this finally results in a splitting of the bond. Let us assume that the P-atom is attacked by an ADP ion. This action results in the formation of a carboxyl ion and the phosphorylation of ADP. (See Fig. 3.) Apparently, the attraction from the O-atom on the σ-electrons of the P–O bond is powerful enough to make the P-atom so positive that it becomes able to attract the electrons of $^-$O–P– in the ADP ion to such a degree that this O-atom becomes a bridge atom at the same time as the P–O bond in the carboxyl-phosphate is broken and the carboxyl ion is formed. Thus it is the powerful attraction from the bridge atom on the σ-electrons which makes possible the simultaneous formation of a carboxyl ion and a new bridge atom, viz. that in ATP.

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[1] This view is consistent with results obtained by Fischer Hjalmars [12] in a complete quantum mechanical calculation of the electron distribution in the O_3 molecule. Fischer-Hjalmars found that, for the O_3 molecule, the effect of the π-electron distribution is diminished considerably by the σ-electron distribution.

In connection with the treatment of the synthesis of acylphosphates, Avison [13] remarks that acyl-phosphoric acids do not react with orthophosphate ions since their negative charge prevents the approach of the attacking phosphate ions. He suggested that, in biological systems in similar reactions, the negative charge can be screened by chelation or in some other way as a result of the enzymic environment. This point of view should be applied to the reactions described in the preceding paragraph. In [3, 4], the present author has suggested that there are balanced forces in the carboxyl-phosphate (in the present paper expressed as the competition for the electrons by the atoms of the –C–O–P– group) and that a small perturbation of this balance by a specific enzyme may render possible a reaction with for example an ADP ion. However, according to Avison's experiments, an attack by a negative ADP ion should be sufficient for reaction. Since the carboxyl-phosphate, which is dissociated, is protected from the attacks of negative ions by its own negative charge, it is very probable that the function of the specific enzyme instead is to render possible the attack by screening the charge of the carboxyl-phosphate. In this way the specific enzymes may be used to control the nature of the attacking ions and thus the anabolism, and it seems probable that the negative charge on the carboxyl-phosphate, protecting against attacks by arbitrary negative ions, makes it especially appropriate for energy transfer in the living cell.

Avison's explanation of the acylation of orthophosphate ions by carboxylic acid anhydrides is different from the present explanation of the phosphorylation of ADP ions even though these reactions are similar. He does not take the charge on the bridge atom into consideration. As appears from the present investigation, it is very probable that this charge is of significant importance for the reaction.

Recently, Clark *et al.* [14] have pointed out the necessity of the heterolysis of the P–O bond in the phosphorylation of ADP and in similar reactions.

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APPENDIX

Table 10. $N(j;\lambda)$ of (16) for each of the lowest space orbitals.

The notation for the atoms is given in Figs. 1 and 2. The numeration of the calculations indicates the types of AO's used and the interatomic distances (see Tables 6 and 7).

(i) *Carboxyl-phosphate*
Calculations I–VI

Calc.	Orb.	O_α	C	O_β	P	$O_{\gamma 1}$	$(O_3)_\gamma$
		A. $2\delta_{OC} = -1.0$ eV; $2\delta_{OP} = -1.4$ eV					
I	1	0.49	0.41	0.09	0.01	0.00	—
	2	0.05	0.00	0.20	0.32	0.42	—
	3	0.10	0.00	0.54	0.00	0.36	—
II	1	0.48	0.40	0.10	0.01	—	0.01
	2	0.05	0.01	0.08	0.35	—	0.51
	3	0.12	0.00	0.69	0.00	—	0.19
III	1	0.44	0.39	0.13	0.03	0.01	—
	2	0.12	0.02	0.21	0.29	0.36	—
	3	0.08	0.00	0.46	0.00	0.46	—
IV	1	0.48	0.40	0.10	0.01	—	0.01
	2	0.05	0.01	0.08	0.35	—	0.51
	3	0.12	0.00	0.69	0.00	—	0.18
V	1	0.44	0.40	0.14	0.02	—	0.01
	2	0.06	0.02	0.08	0.34	—	0.50
	3	0.17	0.00	0.63	0.00	—	0.20
VI	1	0.40	0.38	0.16	0.03	0.03	—
	2	0.11	0.03	0.07	0.29	0.50	—
	3	0.16	0.00	0.61	0.00	0.23	—
		B. $2\delta_{OC} = -1.4$ eV; $2\delta_{OP} = -1.8$ eV					
III	1	0.51	0.37	0.10	0.01	0.01	
	2	0.09	0.01	0.27	0.24	0.39	
	3	0.06	0.00	0.47	0.00	0.47	
		C. $2\delta_{OC} = -1.6$ eV; $2\delta_{OP} = -1.8$ eV					
III	1	0.54	0.35	0.09	0.01	0.01	
	2	0.09	0.01	0.28	0.24	0.38	
	3	0.05	0.00	0.47	0.00	0.47	
		D. $2\delta_{OC} = -2.0$ eV; $2\delta_{OP} = -2.2$ eV					
III	1	0.65	0.32	0.02	0.00	0.00	
	2	0.03	0.00	0.38	0.18	0.41	
	3	0.02	0.00	0.49	0.00	0.49	

Table 10 (*continued*)

(ii) *Carboxyl ion*
Calculation VII

Orb.	O_α	C	O_β
	A. $2\delta_{OC} = -1.0$ eV		
1	0.29	0.42	0.29
2	0.50	0.00	0.50
	B. $2\delta_{OC} = -1.4$ eV		
1	0.31	0.38	0.31
2	0.50	0.00	0.50
	C. $2\delta_{OC} = -1.6$ eV		
1	0.32	0.37	0.32
2	0.50	0.00	0.50
	D. $2\delta_{OC} = -2.0$ eV		
1	0.34	0.33	0.34
2	0.50	0.00	0.50

(iii) *Phosphate ion*
Calculations VIII and IX

Calc.	Orb.	O_β	P	$O_{\gamma 1}$	$(O_3)_\gamma$
		A. $2\delta_{OP} = -1.4$ eV			
VIII	1	0.20	0.38	—	0.42
	2	0.68	0.00	—	0.32
		A. $2\delta_{OP} = -1.4$ eV			
IX	1	0.34	0.32	0.34	
	2	0.50	0.00	0.50	
		B = C. $2\delta_{OP} = -1.8$ eV			
	1	0.37	0.26	0.37	
	2	0.50	0.00	0.50	
		D. $2\delta_{OP} = -2.2$ eV			
	1	0.41	0.19	0.41	
	2	0.50	0.00	0.50	

(iv) *Adenosine diphosphate*
Calculation X

Orb.	O_a	P	O_{b1}	P	O_c
	A. $2\delta_{OP} = -1.4$ eV				
1	0.19	0.17	0.28	0.17	0.19
2	0.35	0.15	0.00	0.15	0.35
3	0.22	0.00	0.57	0.00	0.22
	B = C. $2\delta_{OP} = -1.8$ eV				
1	0.23	0.14	0.25	0.14	0.23
2	0.38	0.12	0.00	0.12	0.38
3	0.18	0.00	0.64	0.00	0.18
	D. $2\delta_{OP} = -2.2$ eV				
1	0.32	0.11	0.15	0.11	0.32
2	0.41	0.09	0.00	0.09	0.41
3	0.10	0.00	0.81	0.00	0.10

Table 10 (*continued*)

(v) *Adenosine triphosphate*
Calculation XI

Orb.	O_a	P	O_{b1}	P	O_c	O_{b2}	P	O_d
	A. $2\delta_{OP} = -1.4$ eV							
1	0.05	0.06	0.17	0.24	0.20	0.17	0.06	0.05
2	0.25	0.16	0.09	0.00	0.00	0.09	0.16	0.25
3	0.23	0.10	0.00	0.10	0.23	0.00	0.10	0.23
4	0.09	0.00	0.23	0.00	0.35	0.23	0.00	0.09
5	0.14	0.00	0.36	0.00	0.00	0.36	0.00	0.14
	B = C. $2\delta_{OP} = -1.8$ eV							
1	0.06	0.05	0.16	0.20	0.25	0.16	0.05	0.06
2	0.29	0.13	0.08	0.00	0.00	0.08	0.13	0.29
3	0.25	0.08	0.00	0.08	0.25	0.00	0.08	0.25
4	0.08	0.00	0.27	0.00	0.31	0.27	0.00	0.08
5	0.11	0.00	0.39	0.00	0.00	0.39	0.00	0.11
	D. $2\delta_{OP} = -2.2$ eV							
1	0.10	0.04	0.10	0.15	0.39	0.10	0.04	0.10
2	0.36	0.10	0.04	0.00	0.00	0.04	0.10	0.36
3	0.27	0.06	0.00	0.06	0.27	0.00	0.06	0.27
4	0.04	0.00	0.37	0.00	0.18	0.37	0.00	0.04
5	0.05	0.00	0.45	0.00	0.00	0.45	0.00	0.05

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